

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

21-490

MICROBIOLOGY REVIEW(S)

Product Quality Microbiology Review

17 October, 2002

Review for HFD-580

NDA: 21-490/N-000-BC

Drug Product Name

Proprietary:

OVCON® 35

Non-proprietary:

norethindrone and ethinyl
estradiol chewable tablets

Drug Product Classification:

Review Number:

2

Subject of this Review

Submission Date:

August 19, 2002

September 10, 2002

October 17, 2002

Receipt Date:

August 27, 2002

September 11, 2002

October 17, 2002

Consult Date:

August 27, 2002

Date Assigned for Review:

September 27, 2002

Submission History (for amendments only)

Date(s) of Previous Submission(s): March 29, 2002

Date(s) of Previous Micro Review(s): June 14, 2002

Applicant/Sponsor

Name:

Warner Chilcott

Address:

Rockaway 80 Corporate Center

100 Enterprise Dr. Suite 280

Rockaway, NJ 07866

Representative:

Ileana Brown

Telephone:

(973) 442-3229

Name of Reviewer:

Stephen E. Langille, Ph.D.

Conclusion:

Recommended for Approval

Product Quality Microbiology Data Sheet

- A. 1. TYPE OF SUPPLEMENT: Amendment to the original submission
2. SUPPLEMENT PROVIDES FOR: N/A
3. MANUFACTURING SITE: Bristol-Myers Squibb
Manufacturing Company
Road 114
Mayaguez, Puerto Rico
00688
4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:
- Chewable Tablet
 - Oral
 - 0.4 mg norethindrone and 0.035 mg ethinyl estradiol per day
5. METHOD(S) OF STERILIZATION: Non-sterile drug product
6. PHARMACOLOGICAL CATEGORY: contraceptive
- B. SUPPORTING/RELATED DOCUMENTS: NDA 17-716
- C. REMARKS: The "non-chewable" tablet was approved in NDA 17-716, OVCON 35 28-day (norethindrone and ethinyl estradiol tablets, USP). The main difference between the new dosage form and the approved product is the addition of a flavor and sweetener, — two excipients (dibasic calcium phosphate, USP and lactose, NF/EP), and — FD&C yellow #6 dye. A deficiency letter was sent to the applicant on July 23, 2002. The Applicant was asked to justify the lack of microbial limits testing on the finished drug product. Responses to this question were provided in documents submitted on August 19, September 10, and October 17 of 2002.

filename: C:/Reviews/ 21-490r2.doc

Executive Summary**I. Recommendations**

- A. Recommendation on Approvability -**
NDA 21-490 is recommended for approval from the standpoint of microbial product quality.
- B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable -**

II. Summary of Microbiology Assessments

- A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology -**
The drug product consists of a non-sterile chewable tablet.
- B. Brief Description of Microbiology Deficiencies -**
No deficiencies were identified based upon the information provided.
- C. Assessment of Risk Due to Microbiology Deficiencies -**
Not applicable

III. Administrative

- A. Reviewer's Signature** _____
- B. Endorsement Block**
In DFS
- C. CC Block**
In DFS

1 Page(s) Withheld

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Stephen Langille
10/18/02 10:24:42 AM
MICROBIOLOGIST

Peter Cooney
10/18/02 01:58:39 PM
MICROBIOLOGIST

Product Quality Microbiology Review

11 June, 2002

Review for HFD-580

NDA: 21-490

Drug Product Name

Proprietary:

OVCON[®] 35

Non-proprietary:

norethindrone and ethinyl
estradiol chewable tablets

Drug Product Classification:

Review Number: 1

Subject of this Review

Submission Date:

March 29, 2002

Receipt Date:

April 2, 2002

Consult Date:

May 17, 2002

Date Assigned for Review:

June 3, 2002

Submission History (for amendments only)

Date(s) of Previous Submission(s):

Date(s) of Previous Micro Review(s):

Applicant/Sponsor

Name:

Warner Chilcott

Address:

Rockaway 80 Corporate Center
100 Enterprise Dr. Suite 280
Rockaway, NJ 07866

Representative:

Alvin Howard

Telephone:

(973) 42-3233

Name of Reviewer:

Stephen E. Langille, Ph.D.

Conclusion:

Approvable pending the
resolution of microbiology
deficiencies

Product Quality Microbiology Data Sheet

- A.
1. TYPE OF SUPPLEMENT: Original Submission
 2. SUPPLEMENT PROVIDES FOR: N/A
 3. MANUFACTURING SITE: Bristol-Myers Squibb
Manufacturing Company
Road 114
Mayaguez, Puerto Rico
00688
 4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:
 - Chewable Tablet
 - Oral
 - 0.4 mg norethindrone and 0.035 mg ethinyl estradiol per day
 5. METHOD(S) OF STERILIZATION: Non-sterile drug product
 6. PHARMACOLOGICAL CATEGORY: contraceptive
- B. SUPPORTING/RELATED DOCUMENTS: NDA 17-716
- C. REMARKS: The "non-chewable" tablet was approved in NDA 17-716, OVCON 35 28-day (norethindrone and ethinyl estradiol tablets, USP). The main difference between the new dosage form and the approved product is the addition of a flavor and sweetener, the — two excipients (dibasic calcium phosphate, USP and lactose, NF/EP), and — FD&C yellow #6 dye.

filename: C:/Reviews/ 21-490r1.doc

Executive Summary**I. Recommendations**

- A. Recommendation on Approvability -**
NDA 21-490 is approvable pending the resolution of microbiological deficiencies.
- B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable -**

II. Summary of Microbiology Assessments

- A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology -**
The drug product consists of a non-sterile chewable tablet.
- B. Brief Description of Microbiology Deficiencies -**
The Applicant did not provide an explanation as to why microbial limits testing will not be conducted on the drug product prior to release.
- C. Assessment of Risk Due to Microbiology Deficiencies -**
Poor manufacturing procedures could lead to unacceptable levels of microbial contamination in the tablets.

III. Administrative

- A. Reviewer's Signature** _____
- B. Endorsement Block**
In DFS
- C. CC Block**
In DFS

2 Page(s) Withheld

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Stephen Langille
6/14/02 11:31:20 AM
MICROBIOLOGIST

Peter Cooney
6/14/02 03:39:07 PM
MICROBIOLOGIST